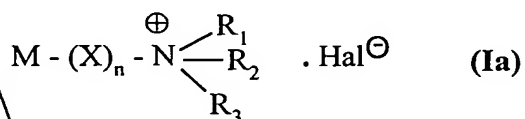


# CLAIMS

## 1- Compounds of formula (Ia) or (Ib) :



wherein :

5 M represents a molecule that can be used for the treatment or diagnosis of pathologies caused by attack on the cartilage,

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>, which may be identical or different, represent a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group,

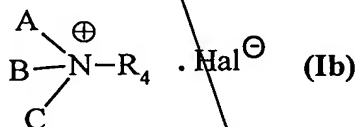
10 or R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>, together with the nitrogen atom carrying them, form a saturated or unsaturated nitrogen-containing heterocycle,

X represents a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkylene chain in which one or more -CH<sub>2</sub>- groups are optionally replaced by a sulphur atom, an oxygen atom, an -NR- group (wherein R represents a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group), a -CO- group, a -CO-NH- group, a -CO<sub>2</sub>- group, an -SO- group or an -SO<sub>2</sub>- group,

15 n represents 0 or 1, and

Hal represents a halogen atom,

or,



R<sub>4</sub> represents a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group,

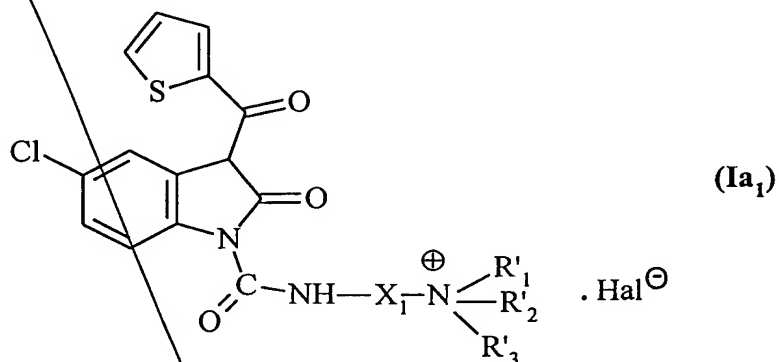
20 Hal represents a halogen atom,

$\begin{matrix} A \\ B \end{matrix} - N$  represents a molecule that can be used for the treatment or diagnosis of pathologies caused by attack on the cartilage, wherein the nitrogen atom may optionally be included in a saturated or unsaturated nitrogen-containing heterocyclic system, or included in a double bond.

## 2- Compound of formula (I) according to claim 1, characterised in that the molecule

M or  $\begin{matrix} A \\ \diagup \\ B-N \\ \diagdown \\ C \end{matrix}$  that can be used for the treatment of pathologies caused by attack on the cartilage is an antiinflammatory, an analgesic, an antiosteoarthritic, an antiarthritic or a specific anti-tumour agent.

3- Compound of formula (I) according to claim 1 as represented by formula (Ia<sub>1</sub>) :



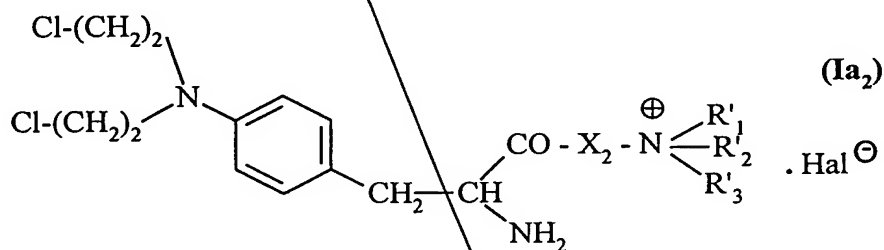
wherein :

X<sub>1</sub> represents a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkylene group,

R'<sub>1</sub>, R'<sub>2</sub> and R'<sub>3</sub>, which may be identical or different, represent a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group, and

Hal represents a halogen atom.

4- Compound of formula (I) according to claim 1 as represented by formula (Ia<sub>2</sub>) :



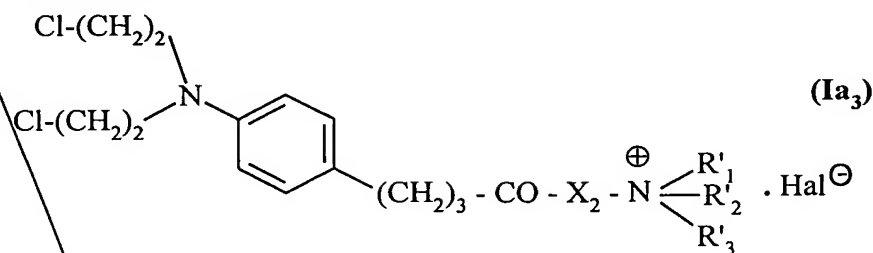
wherein :

X<sub>2</sub> represents a group -NH-(CH<sub>2</sub>)<sub>m</sub>- wherein m represents an integer from 1 to 5 inclusive,

R'<sub>1</sub>, R'<sub>2</sub> and R'<sub>3</sub>, which may be identical or different, represent a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group, and

Hal represents a halogen atom.

5- Compound of formula (I) according to claim 1 as represented by formula (Ia<sub>3</sub>) :



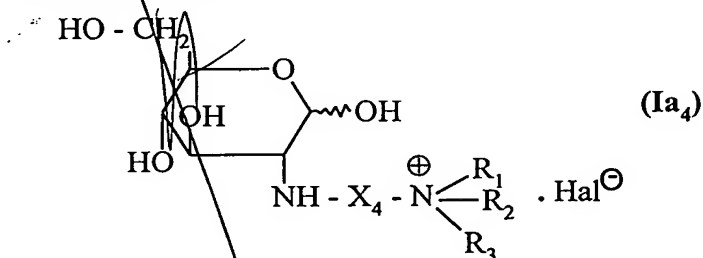
wherein :

X<sub>2</sub> represents a group -NH-(CH<sub>2</sub>)<sub>m</sub>- wherein m represents an integer from 1 to 5 inclusive,

R'<sub>1</sub>, R'<sub>2</sub> and R'<sub>3</sub>, which may be identical or different, represent a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group, and

Hal represents a halogen atom.

6- Compound of formula (I) according to claim 1 as represented by formula (Ia<sub>4</sub>) :



wherein :

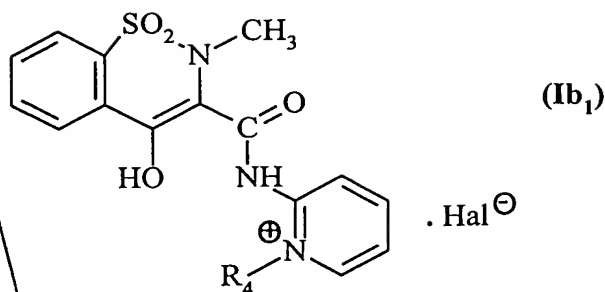
X<sub>4</sub> represents a group -CO-(CH<sub>2</sub>)<sub>m</sub>- wherein m represents an integer from 1 to 5 inclusive,

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>, which may be identical or different, represent a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group,

or R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>, together with the nitrogen atom carrying them, form a saturated or unsaturated nitrogen-containing heterocycle, and

Hal represents a halogen atom.

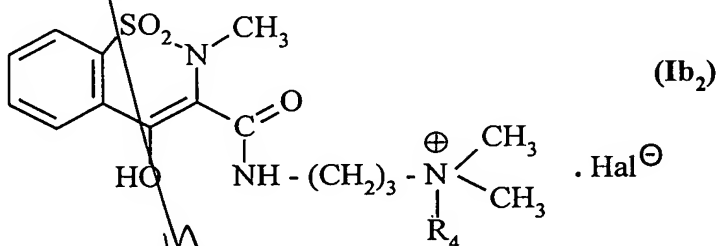
7- Compound of formula (I) according to claim 1 as represented by formula (Ib<sub>1</sub>) :



wherein :

R<sub>4</sub> represents a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group, and  
Hal represents a halogen atom.

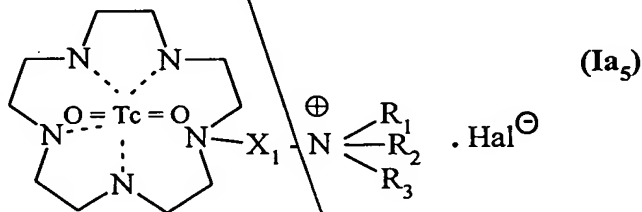
5 8- Compound of formula (I) according to claim 1 as represented by formula (Ib<sub>2</sub>) :



wherein :

R<sub>4</sub> represents a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group, and  
Hal represents a halogen atom.

10 9- Compound of formula (I) according to claim 1 as represented by formula (Ia<sub>5</sub>) :



wherein :

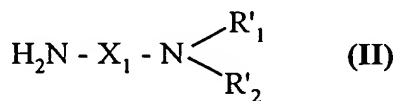
X<sub>1</sub> represents a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkylene group,

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>, which may be identical or different, represent a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group,

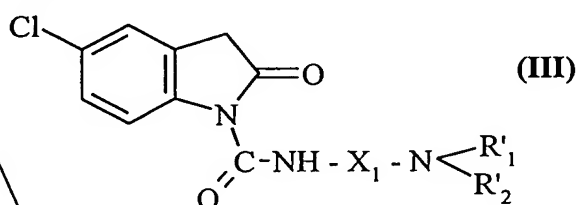
or R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>, together with the nitrogen atom carrying them, form a saturated or unsaturated nitrogen-containing heterocycle, and

Hal represents a halogen atom.

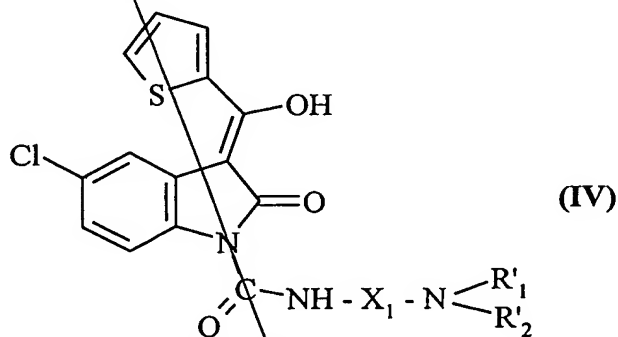
**10-** Process for the preparation of compounds of formula (Ia<sub>1</sub>) according to claim 3, characterised in that they are obtained starting from 4-nitrophenyl 5-chloro-2,3-dihydro-2-oxo-1*H*-indole-1-carboxylate, which is reacted with an amine of formula **(II)** :



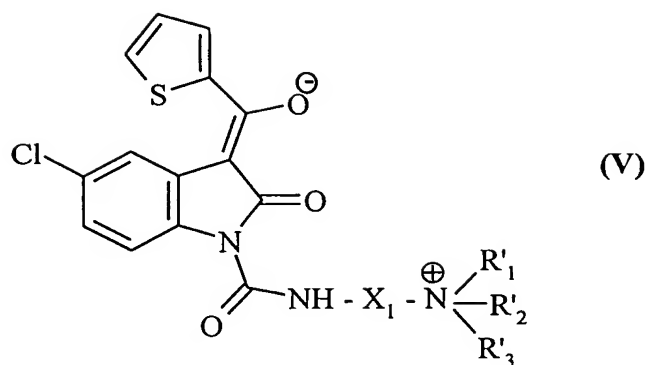
wherein X<sub>1</sub>, R'<sub>1</sub> and R'<sub>2</sub> are as defined in claim 3,  
to yield a compound of formula **(III)** :



wherein X<sub>1</sub>, R'<sub>1</sub> and R'<sub>2</sub> are as defined hereinbefore,  
which is subjected to the action of 2-thienoyl chloride in basic medium under an inert atmosphere, then to treatment with an acid,  
to yield a compound of formula **(IV)** :

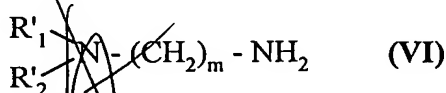


wherein X<sub>1</sub>, R'<sub>1</sub>, and R'<sub>2</sub> are as defined hereinbefore,  
which is converted into the corresponding sodium salt,  
which is then subjected to the action of a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl halide of formula R'<sub>3</sub>Hal (wherein R'<sub>3</sub> is as defined hereinbefore and Hal represents a halogen atom),  
to yield a compound of formula **(V)** :

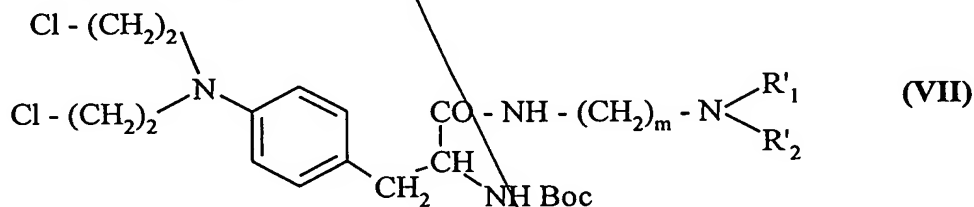


wherein  $X_1$ ,  $R'_1$ ,  $R'_2$  and  $R'_3$  are as defined hereinbefore,  
which, in hydrochloric medium, yields a compound of formula (Ia<sub>1</sub>), which if necessary is purified.

**11-** Process for the preparation of compounds of formula (Ia<sub>2</sub>) according to claim 4, characterised in that they are obtained starting from melphalan, the amine function of which has been protected beforehand by a *tert*-butoxycarbonyl group (Boc), using an amine of formula (VI) in the presence of a peptide coupling reagent :



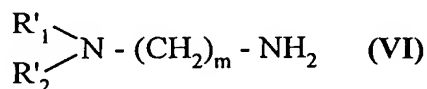
wherein  $R'_1$ ,  $R'_2$  and  $m$  are as defined in claim 4,  
to yield a compound of formula (VII) :



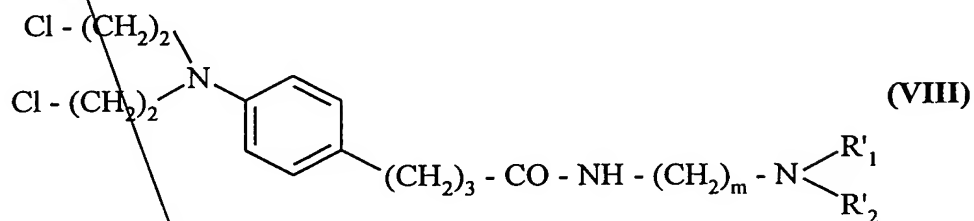
wherein  $m$ ,  $R'_1$  and  $R'_2$  are as defined hereinbefore,  
which is subjected to the action of a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl halide of formula  $R'_3\text{Hal}$  (wherein  $R'_3$  is as defined hereinbefore and Hal represents a halogen atom), then to treatment with HCl,  
to yield a compound of formula (Ia<sub>2</sub>), which if necessary is purified.

**12-** Process for the preparation of compounds of formula (Ia<sub>3</sub>) according to claim 5, characterised in that they are obtained starting from chlorambucil, the acid function of

which is converted into the corresponding acid chloride,  
which is then reacted with an amine of formula (VI), in the presence or absence of a peptide coupling reagent :



wherein  $\text{R}'_1$ ,  $\text{R}'_2$  and  $m$  are as defined in claim 5,  
to yield a compound of formula (VIII) :

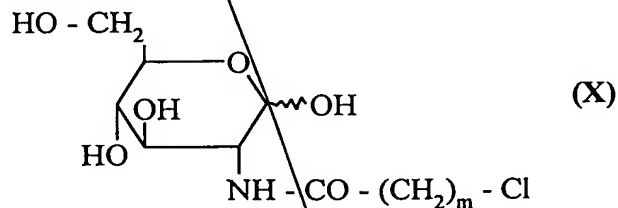


wherein  $m$ ,  $\text{R}'_1$  and  $\text{R}'_2$  are as defined hereinbefore,  
which is subjected to the action of a linear or branched ( $\text{C}_1$ - $\text{C}_6$ )alkyl halide of formula  $\text{R}'_3\text{Hal}$  (wherein  $\text{R}'_3$  is as defined hereinbefore and Hal represents a halogen atom),  
to yield a compound of formula (Ia<sub>2</sub>), which if necessary is purified.

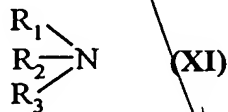
**13-** Process for the preparation of compounds of formula (Ia<sub>4</sub>) according to claim 6,  
characterised in that they are obtained by reaction of glucosamine with an acid chloride of formula (IX) :



wherein  $m$  is as defined in claim 6,  
to yield a compound of formula (X) :

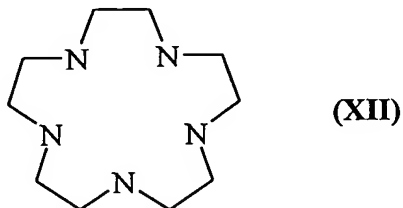


wherein  $m$  is as defined hereinbefore,  
which is condensed with an amine of formula (XI) :

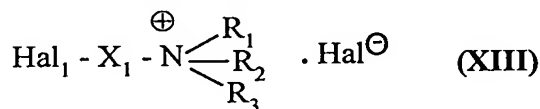


wherein  $R_1$ ,  $R_2$  and  $R_3$  are as defined in claim 6,  
to yield a compound of formula (Ia<sub>4</sub>), which if necessary is purified and which is optionally separated into its isomers according to a conventional separation technique.

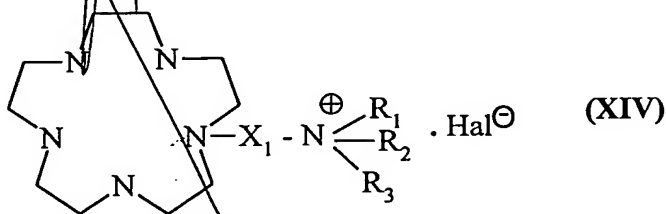
**14-** Process for the preparation of compounds of formula (Ia<sub>5</sub>) according to claim 9,  
characterised in that they are obtained starting from the compound of formula (XII) :



which is reacted with a haloalkylammonium halide of formula (XIII) :



wherein  $X_1$ ,  $R_1$ ,  $R_2$  and  $R_3$  are as defined in claim 9, and Hal and Hal<sub>1</sub>, which may be identical or different, represent halogen atoms  
to yield a compound of formula (XIV) :



wherein  $X_1$ ,  $R_1$ ,  $R_2$ ,  $R_3$  and Hal are as defined hereinbefore,  
which is reacted with sodium pertechnetate in the presence of tin chloride,  
to yield a compound of formula (Ia<sub>5</sub>), which if necessary is purified.

**15-** Process for the preparation of compounds of formula (Ib<sub>1</sub>) according to claim 7,  
characterised in that they are obtained starting from piroxicam, which is reacted with a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl halide, and are if necessary purified.

**16-** Process for the preparation of compounds of formula (Ib<sub>2</sub>) according to claim 8,  
characterised in that they are obtained starting from the corresponding amine, which is



reacted with a linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl halide, and are if necessary purified.

17- Pharmaceutical composition comprising as active ingredient a compound according to any one of claims 1 to 9, alone or in combination with one or more pharmaceutically acceptable, inert, non-toxic excipients or carriers.

5     18- Pharmaceutical composition according to claim 17, comprising a compound according to any one of claims 1 to 8, for use in the treatment of pathologies caused by attack on the cartilage.

10     19- Pharmaceutical composition according to claim 17, comprising a compound according to one of claims 1 or 9, for use as a diagnostic reagent capable of revealing a pathology of the cartilage or a metabolism.

add  
A1

205220 40861001